PCT/GB 2004 / 0 0 4 7 6 0

The Patent Office
PATENTS • DESIGNS • COPYRIGHT • TRADE MARKS

INVESTOR IN PEOPLE

The Patent Office
Concept House
Cardiff Road
Newport
South Wales
NP10 8QQ

REC'D 14 DEC 2004
WIPO PCT

PRIORITY DOCUMENT

SUBMITTED OR TRANSMITTED IN COMPLIANCE WITH RULE 17.1(a) OR (b)

I, the undersigned, being an officer duly authorised in accordance with Section 74(1) and (4) of the Deregulation & Contracting Out Act 1994, to sign and issue certificates on behalf of the Comptroller-General, hereby certify that annexed hereto is a true copy of the documents as originally filed in connection with the patent application identified therein.

I also certify that the attached copy of the request for grant of a Patent (Form 1/77) bears an amendment, effected by this office, following a request by the applicant and agreed to by the Comptroller-General.

In accordance with the Patents (Companies Re-registration) Rules 1982, if a company named in this certificate and any accompanying documents has re-registered under the Companies Act 1980 with the same name as that with which it was registered immediately before re-registration save for the substitution as, or inclusion as, the last part of the name of the words "public limited company" or their equivalents in Welsh, references to the name of the company in this certificate and any accompanying documents shall be treated as references to the name with which it is so re-registered.

In accordance with the rules, the words "public limited company" may be replaced by p.l.c., plc, P.L.C. or PLC.

Re-registration under the Companies Act does not constitute a new legal entity but merely subjects the company to certain additional company law rules.

Signed AMBrewer.

Dated 23 November 2004

BEST AVAILABLE COPY

GB 0326381.1

By virtue of a direction given under Section 30 of the Patents Act 1977, the application is proceeding in the name of:

THE INSTITUTE OF CANCER RESEARCH:ROYAL CANCER HOSPITAL,
123 Old Brompton Road,
LONDON,
SW7 3RP,
United Kingdom

Incorporated in the United Kingdom,

[ADP No. 03969045003]

and

THE ROYAL MARSDEN NHS FOUNDATION TRUST,
Downs Road,
SURREY,
SM2 5PT,
United Kingdom

Incorporated in the United Kingdom,

[ADP No. 08977936001]

Patents Form 1/77

Patents Act 1977
(Rule 16)

THE PATENT OFFICE
12 NOV 2003
RECEIVED BY HAND

The Patent Office

13NOV03 E851640-2 D00060
P01/7700 0.00-0326381.1

Request for grant of a patent

(See the notes on the back of this form. You can also get an explanatory leaflet from the Patent Office to help you fill in this form)

The Patent Office

Cardiff Road
Newport
South Wales
NP10 8QQ

1. Your reference

ASF/BP6183248

2. Patent application number
(The Patent Office will fill this part in)

0326381.1

12 NOV 2003

3. Full name, address and postcode of the or of each applicant *(underline all surnames)*

THE INSTITUTE OF CANCER RESEARCH: Royal Cancer Hospital
123 OLD BROMPTON ROAD
LONDON
SW7 3RP

Patents ADP number *(if you know it)*

SECTION 30 (1977 ACT) APPLICATION FILED 26/10/04

8173940001

If the applicant is a corporate body, give the country/state of its incorporation

UNITED KINGDOM

4. Title of the invention

A METHOD AND MEANS FOR IMAGE PROCESSING

5. Name of your agent *(if you have one)*

"Address for service" in the United Kingdom to which all correspondence should be sent
(including the postcode)

MEWBURN ELLIS LLP
York House
23 Kingsway
London WC2B 6HP

Patents ADP number *(if you know it)*

~~109006~~ 8836884001

6. Priority: Complete this section if you are declaring priority from one or more earlier patent applications, filed in the last 12 months.

Country	Priority application number *(if you know it)*	Date of filing *(day / month / year)*

7. Divisionals, etc: Complete this section only if this application is a divisional application or resulted from an entitlement dispute (see note f)

Number of earlier UK application	Date of filing *(day / month / year)*

8. Is a Patents Form 7/77 (Statement of inventorship and of right to grant of a patent) required in support of this request?

YES

Answer YES if:
a) any applicant named in part 3 is not an inventor, or
b) there is an inventor who is not named as an applicant, or
c) any named applicant is a corporate body.
Otherwise answer NO (See note d)

9. Accompanying documents: A patent application must include a description of the invention. Not counting duplicates, please enter the number of pages of each item accompanying this form:

Continuation sheets of this form	0
Description	44
Claim(s)	14
Abstract	0
Drawing(s)	6 +6

CF

10. If you are also filing any of the following, state how many against each item.

Priority documents	0
Translations of priority documents	0
Statement of inventorship and right to grant of a patent (Patents Form 7/77)	0
Request for a preliminary examination and search (Patents Form 9/77)	0
Request for a substantive examination (Patents Form 10/77)	0
Any other documents (please specify)	0

11. I/We request the grant of a patent on the basis of this application.

Signature(s) Newburn Ellis Date 11 NOVEMBER 2003

12. Name, daytime telephone number and e-mail address, if any, of person to contact in the United Kingdom Andrew S. FEARNSIDE 0161 247 7722

Warning

After an application for a patent has been filed, the Comptroller of the Patent Office will consider whether publication or communication of the invention should be prohibited or restricted under Section 22 of the Patents Act 1977. You will be informed if it is necessary to prohibit or restrict your invention in this way. Furthermore, if you live in the United Kingdom, Section 23 of the Patents Act 1977 stops you from applying for a patent abroad without first getting written permission from the Patent Office unless an application has been filed at least 6 weeks beforehand in the United Kingdom for a patent for the same invention and either no direction prohibiting publication or communication has been given, or any such direction has been revoked.

Notes

a) If you need help to fill in this form or you have any questions, please contact the Patent Office on 08459 500505.

b) Write your answers in capital letters using black ink or you may type them.

c) If there is not enough space for all the relevant details on any part of this form, please continue on a separate sheet of paper and write "see continuation sheet" in the relevant part(s). Any continuation sheet should be attached to this form.

d) If you have answered YES in part 8, a Patents Form 7/77 will need to be filed.

e) Once you have filled in the form you must remember to sign and date it.

f) Part 7 should only be completed when a divisional application is being made under section 15(4), or when an application is being made under section 8(3), 12(6) or 37(4) following an entitlement dispute. By completing part 7 you are requesting that this application takes the same filing date as an earlier UK application. If you want the new application to have the same priority date(s) as the earlier UK application, you should also complete part 6 with the priority details.

A method and means for image processing

The present invention relates to methods and means for image processing and, particularly, though not exclusively, to the processing of Nuclear Magnetic Resonance image data.

Dynamic imaging, such as dynamic MR imaging, may involve the acquisition of a time-series of image data sets in which each data set is able to represent an image of the subject fully in 2 or 3 dimensions at one of a series of successive instants (or brief periods) in time. Dynamic imaging is often used to record the internal changes in properties of a stationary subject which are induced by a controlled change-inducing influence. An example of this is contrast-enhanced medical MR imaging in which a "contrast agent" is introduced into a stationary subject (e.g. a person) which is detectable as an increase in the image contrast/brightness of those internal parts of the subject in which the agent is located.

An analysis of the change in image properties (e.g. in image contrast/brightness), over time, of chosen fixed points or static regions within the imaged volume of the

subject enables an assessment of the properties of the chosen fixed points/regions within that imaged volume.

For example, the image analysis procedure in breast dynamic imaging typically involves localisation of a lesion within an image of the subject containing a contrast agent. According to present image analysis procedures, the pixel value of each pixel within an image of the subject containing a contrast agent (post-contrast images) has subtracted from it the pixel value of the corresponding pixel located at the same image point within an image of the same subject taken prior to introduction of the contrast agent thereto (pre-contrast image). The result is a "subtraction image" which ideally includes only the effects of the contrast agent upon the subject.

In many situations the image subject (e.g. region of a body, such as a breast) contains a high content of material (e.g. fat) other than the material of interest which may obscure relevant image features (e.g. lesion shape features) within a post-contrast image. This is especially so in breast-scan images. While the technique of generating subtraction images aims to remove the contribution to, or part of, the image arising from fat (and other materials to which the use of the contrast

agent was not directed), this can never be fully achieved due to the fact that materials (especially fat) other than the material of interest may often also be enhanced to a small extent by the presence of a contrast agent. Thus, even a subtraction image is likely to suffer the obscuring effects discussed above arising from undesired image contrast enhancement.

Analysis of lesion shape within an image and of the pattern of enhancement due to contrast agent uptake may make a valuable contribution to diagnosis. The analysis of lesion shape can only be considered reliable in cases where the tumour extent is properly segmented within the image being studied. The "traditional" approach to this problem is manual segmentation of the tumour region within subtraction images (e.g. by a radiologist). Even if the shape obscuring tissue is not enhancing, it cannot be eliminated using the subtraction technique because of noise present in the pre-contrast and/or post-contrast image data. As a result the tumour-outlining contour so produced is not always well defined.

Moreover, merely segmenting the outlining image contour of a tumour image may not be satisfactory/sufficient if the tumour in question has a heterogeneous structure, which is not clearly seen on a subtracted image. As a

result the pattern of contrast enhancement is not always clearly seen on the subtraction image. Furthermore, a subtraction image alone does not always permit one to discriminate between tumour and other enhancing tissues, e.g. blood vessels.

The present invention aims to overcome at least some of the above deficiencies of the prior art.

The present invention, at its most general, proposes to provide a method and/or means enabling one to identify in an image, being one of a time-sequence of images recording induced changes in pixel values of successive images of a subject (such as post-contrast dynamic images), the contribution to the image arising from the presence within the image subject of a specified material/tissue (such non-enhancing and/or low-enhancing material, e.g. fat). This identification is proposed to be done using a statistical measure derived from the dynamic data (e.g. pixel value changes due to contrast agent uptake) taken from a plurality of the separate images forming the time-sequence.

In the case of a time-sequence of images recording the development of contrast-enhancement in a subject, this is preferably done in respect of individual image pixels (or

"voxels" in a 3D image) from information contained in the pixel intensity data recording the contrast enhancement of the subject at a point or pixel location therein. Thus, the statistical measure is most preferably derived according to the variation over time of the pixel intensity at an individual image pixel location (i.e. the "uptake curves" representing contrast enhancement due to contrast agent uptake over time at a given imaged point).

The pixel intensity of a given pixel changes over time either predominantly in response to a deliberate induced effect (e.g. the presence of a contrast enhancing agent) at the location within the subject represented by the pixel, and/or due to image noise. Different material/tissue types respond differently to the presence of a contrast enhancing agent and the present invention proposes a method and means for utilising this fact in identifying different materials within the image of a subject, using a statistical measure if the induced image pixel value changes (over time) which has been found to be material-specific.

It is to be understood that the present invention is not limited to the processing of Nuclear Magnetic Resonance image data and is applicable to the processing of image

data acquired via other means and in respect of any subject.

Accordingly, in a first of its aspects, the present invention may provide a method of processing a time-sequence of separate image data sets which record induced changes in pixel values of successive images of a subject, each set comprising a plurality of image data items which each represent the location of an image pixel of the image subject according to a common reference frame within which the subject is located, the method including the steps of:

(a) selecting from each of a plurality of the separate image data sets an image data item which represents an image pixel located at the same fixed image pixel location, thereby to generate a time-domain image data set;

(b) determining according to a predetermined measure of said induced changes as between the pixel values of the image data items of the time-domain image data set whether the image data items thereof are associated with the presence of a specified material within the image subject.

There may then follow an additional step (c), following step (b), of identifying or classifying the image data

items of the time-domain image data set as being unsuitable for use in the generation of an image of the subject if they are identified in step (b) as being associated with the presence of the specified material within the image subject and if the specified material is of a type which it is not desired to be included within the image of the subject. Otherwise, the image data items in question may be identified/classified as being suitable for use in image generation of the subject.

Thus, the time-domain image data set contains information regarding exclusively the image pixels representing the same location within the common reference frame of each of the plurality of successive images in the time-sequence of images. By analysing the information contained in this dynamic time-domain image data set, one is able to derive information in respect of any one of the plurality of separate image data sets within the time-sequence which would not be derivable from that one image data set alone - namely, whether a pixel value therein results from a specified material (e.g. fat) within the image subject, or otherwise.

The predetermined measure of the induced effect may be any one of a number of measures, which enable, from an analysis of the time-development of the intensity value

of a pixel at the same location within each of the separate images in the time-sequence, whether that development arose predominantly due to a specific material (e.g. fat). Such measures as would be readily apparent to the skilled person may be employed according to the present invention.

Where the pixel location of an image is non-responsive or only weakly responsive to an inducement to changes in its pixel value, when the imaged subject is exposed to a deliberate change-inducing influence or agent, the value of the pixel at that location is likely to be the same (or similar) in each of the images within the time-sequence. Conversely, if the location is strongly responsive to such inducements to changes in its pixel value, the value of the pixel at that location is likely to change significantly over time within the time sequence.

Accordingly, the predetermined measure is most preferably defined according to a measure of the dispersion of, or differences between, the values of pixel intensity associated with the image data items within the time-domain image data set. If only a small degree of difference (as between values) in such pixel intensity

values exists when considering all pixel values represented within the time-domain image data set, this amounts to a small dispersion in pixel intensity values and suggests the observed dispersion results from the pixel values representing material (e.g. fat) within the imaged subject which is non-responsive or only weakly responsive to the inducements to change. The image data items of the time-domain image data set may be so classified and may be identified as being not suitable for use in the generation of an image of the subject. Conversely, large values of dispersion suggest the observed dispersion arises from materials strongly responsive to the inducement to change and may be so classified. These image data items of the time-domain image may also be classified as being suitable for use in the generation of an image of the subject.

Preferably, the image data items of the time-domain image are determined as being associated with the presence within the image subject of the specified material if the predetermined measure exceeds a predetermined threshold value. Preferably, the predetermined threshold is a value of the measure of dispersion in the values of pixel intensity associated with the image data items within the time-domain image data set.

For example, the measure of dispersion may be determined according to the extent to which the pixel values represented by the image data items of the time-domain image data set differ from equality (i.e. the extent to which they do not all share the same value). To this extent, the measure of dispersion may be determined according to the degree to which a time-domain image vector differs from an identity vector in the same vector space, wherein each vector component of the time-domain image vector is represented by a unique image data item of the time-domain image data set, the array of vector components being arranged in time-sequence, and all vector components of the identity vector share the same value (preferably, the value 1 (one)). The degree of difference (and therefore the measure of dispersion) may be the angle subtended by the time-domain image vector with respect to the identity vector. Indeed, the measure of dispersion may be determined according to any suitable property of the time-domain vector in vector space. Preferably, the property in question is a property of the vector as a whole (e.g. its angle relative to another as above).

For example, step (b) of the method of the present invention in its first aspect may include:

forming a time-domain image vector wherein each image data item of the time-domain image data set represents a separate vector component of an array of vector components arranged in the time-sequence to form the time-domain image vector;

determining the angle (α) subtended by the time-domain image vector with respect to the identity vector in the vector space of the time-domain image vector; and,

employing the angle (α) as the predetermined measure, wherein the predetermined threshold value is a predetermined value of the predetermined measure.

Alternatively, the measure of dispersion in the values of pixel intensity associated with the image data items within the time-domain image data set may be determined according to a property or properties of one or more of the principal components of the time-domain image vector determined according to a principal component decomposition of the time-domain image vector.

It has been found that the value of the second principal component (that is, the principal component associated with the second largest eigenvalue of the Principal Component Analysis (PCA)) provides a reliable measure of the dispersion in the values of pixel intensity associated with the image data items within the time-

domain image data set. Preferably, the predetermined threshold is a predetermined value of the second principal component of the time-domain image vector. Preferably, the predetermined threshold value is exceeded if the value of the second principal component is greater than zero.

For example, step (b) may include:

forming a time-domain image vector wherein each image data item of the time-domain image data set represents a separate vector component of an array of vector components arranged in the time-sequence to form the time-domain image vector;

determining the second principal component of the time-domain image vector; and,

employing the value of the second principal component as the predetermined measure, wherein the predetermined threshold value is a predetermined value of the predetermined measure.

Where step (b) includes the calculation of the angle (α) the predetermined threshold value may be deemed to be exceeded if the angle (α) is less than a threshold angle value (α_0). The threshold value (α_0) may be arbitrarily set by the user, but is preferably determined according to the distribution of the angular values (α) of the

time-domain image vectors associated with a plurality of (preferably all of) the image pixel locations represented in the time-sequence of data sets.

The method may include:

repeating step (a) in respect of a plurality of image data items thereby to generate a corresponding plurality of time-domain image data sets;

forming a corresponding plurality of time-domain image vectors with each image data item of a given time-domain image data set representing a separate vector component of an array of vector components arranged in the time-sequence to form the given time-domain image vector;

determining the angle subtended by each of the time-domain image vectors with respect to the identity vector in the vector space of the time-domain image vector; and,

determining from the distribution of the values of the angles (preferably the values of the natural logarithm of the angles) of all of the time-domain vectors the portion of the angular distribution arising mainly, predominantly, or substantially only from the presence of the specified material within the image subject. The predetermined threshold value may then be deemed to be exceeded if the angle subtended by the time-domain image vector falls within, or contributes to, the

portion of the angular distribution arising from the specified material (e.g. fat).

Preferably, the threshold angle value (α_0) is the angular value which demarcates the portion of the angular distribution arising mainly, predominantly, or substantially only from the specified material from the other portion(s) of the angular distribution. For example, the portion of the angular distribution arising mainly, predominantly, or substantially only from the specified material may be determined according to a Normal Distribution having distribution parameters which cause it to most closely correspond with a portion of the angular distribution. Demarcation may be performed graphically/visually, or may be performed analytically and automatically using, for example, the well-known ROC technique in a manner such as would be readily apparent to the skilled person ("Receiver Operating Characteristics": see D J Fink and D Christiansen, Electronic Engineer's Handbook, McGraw-Hill, 3rd edition (1989), section 25, pp119-120).

The method of processing image data, in its first aspect, preferably includes the additional step of:

(d) replacing by a value of zero the pixel value of each image data item of each of the plurality of the

separate image data sets identified as being unsuitable for use in the generation of an image of the subject. In this way, separate image data sets of the time-sequence may be processed to remove material-specific pixels values therefrom leaving unchanged only those pixels which have been processed only if they have been deemed suitable for use in image formation.

Furthermore, the removal of noise from the image data may be achieved by decomposing according to a principal value decomposition the/each time-domain image vector which has been deemed suitable for use in image formation, and discarding from the decomposed vector those principal components which are deemed to arise predominantly from random causes.

For example, the method may also include representing the time-domain image vector in terms of a principal component decomposition thereof employing all principal component vectors and corresponding principal component values thereof except: those principal component values thereof not exceeding a predetermined magnitude; and,

replacing by a value determined according to the principal component decomposition the pixel value of each image data item of each of the plurality of the separate

image data sets identified as being suitable for use in the generation of an image of the subject.

However, it has also been found that the first (largest) principal component of a time-domain image vector generally corresponds to the image data common to all images of the time-sequence. Thus, in the case where the time-sequence records contrast enhancement beginning with a pre-contrast image, the first principal component of each time-domain image vector of the sequence approximately represents the information contained within the pre-contrast image data set, that being the first set within the time-sequence. Subtraction of this information from the time-domain image vectors will result in the maximisation of the differences between different time-domain image vectors (e.g. uptake curves) by removing the information which is common to all time-domain image vectors (e.g. uptake curves). The term "subtraction" is to be understand to refer to the reconstruction of a vector using its principal components except (i.e. omitting) its 1st principal component.

Thus, the method may also include representing the time-domain image vector in terms of a principal component decomposition thereof employing all principal component vectors and corresponding principal component values

thereof except: those principal component values thereof not exceeding a predetermined magnitude; and/or the largest principal component value thereof; and,

replacing by a value determined according to the principal component decomposition the pixel value of each image data item of each of the plurality of the separate image data sets identified as being suitable for use in the generation of an image of the subject.

Preferably, the method of processing according to the invention in its first aspect, includes repeating steps (a) and (b), or steps (a) to (c), (including any of the preferable/alternative features described above) in respect of pixels at each pixel location represented within the time-sequence of separate image data sets. Thus, preferably all image pixels are processed as above. Of course, the present invention may provide a method of forming an image from image data comprised in the time-sequence of separate image data sets having been processed according to the invention in its first aspect (including any of the preferable/alternative features described above).

It is to be understood that the present invention may provide means arranged to, or suitable for, the implementation of the invention in its first aspect.

Accordingly, it is to be understood that the present invention encompasses such means.

For example, in a second of its aspects, the present invention may provide an image processing means for processing a time-sequence of separate image data sets which record induced changes in pixel values of successive images of a subject, each set comprising a plurality of image data items which each represent the location of an image pixel of the image subject according to a common reference frame within which the subject is located, the image processing means including:

(a) selection means for selecting from each of a plurality of the separate image data sets an image data item which represents an image pixel located at the same fixed image pixel location, thereby to generate a time-domain image data set;

(b) decision means for determining according to a predetermined measure of said induced changes as between the pixel values of the image data items of the time-domain image data set whether the image data items thereof are associated with the presence of a specified material within the image subject.

The apparatus may also include:

(c) identifying means arranged to identify or classify the image data items of the time-domain image data set as being unsuitable for use in the generation of an image of the subject if they are identified by said decision means (b) as being associated with the presence of the specified material within the image subject and if the specified material is of a type which it is not desired to be included within the image of the subject. The identifying means may be arranged to otherwise identify the image data items in question as being suitable for use in image generation of the subject.

Preferably, the decision means is arranged to determine that the image data items of the time-domain image are associated with the specified material if the predetermined measure exceeds a predetermined threshold value. Preferably, the predetermined threshold is a predetermined value of the measure of dispersion in the values of pixel intensity associated with the image data items within the time-domain image data set.

To this extent, the measure of dispersion may be determined according to the degree to which a time-domain image vector differs from an identity vector in the same vector space, wherein each vector component of the time-domain image vector is represented by a unique image data

item of the time-domain image data set, the array of vector components being arranged in time-sequence, and all vector component of the identity vector share the same value. The degree of difference (and therefore the measure of dispersion) may be the angle subtended by the time-domain image vector with respect to the identity vector.

The decision means may include:

vector means for forming a time-domain image vector wherein each image data item of the time-domain image data set represents a separate vector component of an array of vector components arranged in the time-sequence to form the time-domain image vector;

angle determining means for determining the angle (α) subtended by the time-domain image vector with respect to the identity vector in the vector space of the time-domain image vector;

wherein the decision means is arranged to employ the angle (α) as the predetermined measure, wherein the predetermined threshold value is a predetermined value of the predetermined measure.

Alternatively, or additionally, the decision means may include:

vector means for forming a time-domain image vector wherein each image data item of the time-domain image data set represents a separate vector component of an array of vector components arranged in the time-sequence to form the time-domain image vector;

principal component means for determining the second principal component of the time-domain image vector;

wherein the decision means is arranged to employ the value of the second principal component as the predetermined measure, wherein the predetermined threshold value is a predetermined value of the predetermined measure. Preferably, the predetermined threshold is exceeded if value of the second principal component is greater than zero.

Where the decision means employs the angle (α), the predetermined threshold value may be deemed to be exceeded if the angle (α) is less than a threshold angle value (α_0).

The selection means is preferably arranged to generate in respect of a plurality of image data items a corresponding plurality of time-domain image data sets;

the vector means is arranged to form a corresponding plurality of time-domain image vectors with each image data item of a given time-domain image data set

representing a separate vector component of an array of vector components arranged in the time-sequence to form the given time-domain image vector;

the angle determining means is arranged to determine the angle subtended by each of the time-domain image vectors with respect to the identity vector in the vector space of the time-domain image vector; and,

the decision means is arranged to determine from the distribution of the values of the angles (preferably the values of the natural logarithm of the angles) of all of the time-domain vectors the portion of the angular distribution arising predominantly, mainly, or substantially only from the presence of the specified material within the image subject. The predetermined threshold value may then be deemed to be exceeded if the angle subtended by the time-domain image vector falls within the portion of the angular distribution arising from the specified material.

Preferably, the threshold angle value (α_0) is the angular value which demarcates the portion of the angular distribution arising substantially only from the specified material from the other portion(s) of the angular distribution.

The decision means may be arranged to determine the portion of the angular distribution arising substantially only from the specified material according to a Normal Distribution having distribution parameters which cause it to most closely correspond with a portion of the angular distribution.

The image processing means of the present invention, in its second aspect, preferably includes:

(d) data modifying means arranged to replace by a value of zero the pixel value of each image data item of each of the plurality of the separate image data sets identified by the identifying means (c) as being unsuitable for use in the generation of an image of the subject.

The principal component means is preferably arranged to represent the time-domain image vector in terms of a principal component decomposition thereof employing all principal component vectors and corresponding principal component values thereof except: the largest principal component value thereof; and those principal component values thereof not exceeding a predetermined magnitude.

The image processing means preferably further includes data modifying means arranged to replace by a value

determined according to the principal component decomposition the pixel value of each image data item of each of the plurality of the separate image data sets identified as being suitable for use in the generation of an image of the subject.

The image processing means of the present invention, according to its second aspect is preferably arranged to process each pixel of each of the time-sequence of separate image data sets.

The image processing means preferably includes image forming means for forming an image from image data comprised in the time-sequence of separate image data sets having been processed by the image processing means according to the invention in its second aspect (including any of the aforementioned preferable/alternative features thereof).

The invention may provide computer means programmed to perform the method according to the invention in its first aspect (including any of the aforementioned preferable/alternative features thereof). The invention may provide a computer program product containing a computer program for performing the method according to the invention in its first aspect (including any of the

aforementioned preferable/alternative features thereof). The invention may provide a computer program for performing the method according to the invention in its first aspect (including any of the aforementioned preferable/alternative features thereof). The invention may provide an image generated according to the method of the invention in its first aspect (including any of the aforementioned preferable/alternative features thereof).

The invention shall now be described in terms of the following non-limiting examples with reference to the accompanying drawings in which:

Figure 1 illustrates the distribution of the natural logarithm of the value of the angle subtended by the time-domain image vectors of each image pixel location of a time-sequence of images relative to the identity vector in the image space of the time-domain image vectors;

Figure 2 illustrates a decomposition of the distribution illustrated in figure 1 into a Normal component most closely corresponding with a Normal Distribution, and a residual component being the difference between the Normal component and the distribution of figure 1;

Figure 3 illustrates a decomposition of the distribution illustrated in figure 1 into two fractions ("fat" and "non fat") discriminated using the value of

the second principal component with threshold value equal to zero;

Figure 4 illustrates the effects upon the distribution of figure 1 of not removing background noise from the distribution (such removal having occurred in the distribution of figure 1);

Figure 5(a) illustrates a sequence of post-contrast images processed according to the present invention (post-contrast time is incrementing from left to right);

Figure 5(b) illustrates a sequence of post-contrast subtraction images according to known methods;

Figure 5(c) illustrates an enlarged first image of the sequence illustrated by figure 5(a)

Figure 6(a) illustrates an image processed according to the present invention;

Figure 6(b) illustrates a post-contrast subtraction image according to known methods.

In the following, the invention shall be illustrated in terms of the processing of a dynamic image data set recording contrast enhancement in a subject containing a high fat content.

Consider a time-sequence of M separate image datasets each of which contains image data elements acquired by Magnetic Resonance Imaging of a subject immediately

before and subsequent to application of an image contrast enhancing agent, and representing the imaged subject in three dimensions (i.e. a volume image). Each volume image is represented as a stack of two-dimensional image frames with lattice dimensions N_x, N_y, N_z (respectively number of columns and rows in a frame, and a stack length), and total number of image pixels (or "voxels" for a volume image) is $N = N_x \times N_y \times N_z$.

Let $\mathbf{Y}_i = (y_{i,1}, \ldots, y_{i,M})$, i = 1, …, N be a time-domain image data set (representing a contrast enhancement agent uptake vector, i.e. the vector representation of an uptake curve of a single voxel) of a single voxel at a fixed image point "i" common to each of the M separate image data sets within the sequence. The time-domain image data set is expressed as a vector in M-dimensional Euclidean space wherein each image data item of the time-domain image data set represents a separate vector component of an array of vector components arranged in said time-sequence to form the time-domain image vector $\mathbf{Y}_i = (y_{i,1}, \ldots, y_{i,M})$.

One may distinguish between non- and low-enhancing tissues, such as fat, and the tissues enhancing to a high extent.

We assume that each uptake vector belongs to a certain class corresponding to a tissue of specific kind. The dispersion/differences in image pixel values of corresponded temporal points of the time-domain image vectors (uptake vectors) from the same class are only due to the random noise. It follows that

$$y_{i,j} \propto Norm\left(\mu_{k,j}, \sigma^2\right), \qquad i \in \Lambda_k$$

Where Λ_k is a set of uptake vectors that build the kth cluster in the Euclidean space within which the time-domain image vectors are defined. The quantity $\mu_{k,j}$ is the expected value of the jth value (temporal point) of an uptake vector that belongs to the kth cluster, and the quantity σ is the standard deviation of the random noise which may, for simplicity, be assumed to be the same for all the dynamic images (this assumption is, however, not necessary).

We shall base our classification on the following model. The dispersion of values of the components ($y_{i,j}$) of an individual time-domain image vector $\mathbf{Y}_i = \left(y_{i,1}, \ldots, y_{i,M}\right)$ (uptake vector) can be modelled by two factors:

(1) contrast enhancement, being induced and due to a deliberate effect, increases the

dispersion of the expected values $\mu_{k,1},\ldots,\mu_{k,M}$ of the corresponded cluster; and,

(2) random noise.

For a cluster representing low enhancing tissue, the difference between the temporal points of an uptake curve is mostly due to noise and so the dispersion of the expectation values $\mu_{k,1},\ldots,\mu_{k,M}$ is small.

It follows that for non-enhancing and low-enhancing tissues the dispersion should be less than is observed in a significantly contrast-enhancing tissue, since the tissue is not subject to a deliberate or significant contrast-enhancing effect, or if there is any such effect it relatively small.

To establish a measure of the enhancement effect, one may find a measure of the dispersion of $\mu_{k,1},\ldots,\mu_{k,M}$. This may be done using the time-domain vector, $\mathbf{Y}_i = \left(y_{i,1},\ldots,y_{i,M}\right)$, and the idem (or "identity") vector, $\mathbf{1}_{1\times M} = \underbrace{(1,\ldots,1)}_{M}$ as follows.

Considering the uptake curves as vectors in M-dimensional Euclidean space (as mentioned above), the smaller the dispersion of the expectation values $\mu_{k,1},\ldots,\mu_{k,M}$, the closer

to the idem vector will lay the vectors of the cluster Λ_k. Thus, the angle (α) subtended by a given time-domain image vector with respect to the idem vector in the vector space of the time-domain image vector is determined and employed as a measure of the degree of dispersion present within that vector. This measure reflects both the enhancement effect and the random noise. The effect of noise should be taken into account. One should find a threshold value α_0. Should an uptake vector posses value $\alpha > \alpha_0$, the uptake vector reflects significant enhancement. Statistically this is equivalent to testing the hypothesis that the vector represents tissue, possessing enhancement bigger than the non- or low responsive material (e.g. fat) Later we describe how to determine the threshold analysing the distribution of the statistics (α).

Assuming that the values of α are small:

$$\alpha_i \approx tg(\alpha_i) = \frac{\sqrt{\frac{1}{M}\sum_{j=1}^{M}\left(y_{i,j} - \bar{y}_{i,\bullet}\right)^2}}{\bar{y}_{i,\bullet}} \qquad (1)$$

Where $\bar{y}_{i,\bullet} = \frac{1}{M}\sum_{j=1}^{M} y_{i,j}$ is the average of the temporal points of the time-domain vector (uptake vector).

The angle (α) is determined in respect of all time-domain image vectors (uptake vectors) of all image pixel points of the image volume thereby to generate a corresponding plurality of such angles. It can be straightforward proven mathematically that the values of α will be approximately log-normally distributed. Each cluster, Λ_k, will possess its own distribution, so for the whole volume one shall have a mixed distribution.

One may determine from the distribution of the values of the angles of all of said time-domain vectors the portion of the angular distribution arising substantially only from the presence within the image subject of a specified low-enhancing tissue (e.g. fat). Once this specified portion has been determined, one may then determine that the contribution to the pixel values of the image data items of a given time-domain image vector (uptake vector) arising from the specified material exceeds a predetermined threshold value if the angle α subtended by that time-domain image vector falls within the specified portion of the angular distribution.

Figure 1 shows an example of the distribution of the values of $\ln(\alpha)$ for a dynamic breast MR measurement (the solid line). One can see that this is a mixed

distribution. One can identify a cluster corresponding to the small values of α (shown by the fitted Normal Distribution (Gaussian) curve - the dashed line). The identified cluster is closer to the idem vector in terms of α, i.e. possessing small enhancement effect. It also represents statistically the most significant and uniform fraction of the population. One may conclude that this cluster represents tissue not significantly responsive to contrast agent, such as fat (at least), within the imaged subject. In general, this cluster represents a tissue that is not highly responsive to the contrast agent and which is not the tissue of interest to which the use of the contrast agent was directed. Hereafter, we shall refer to the identified cluster as a "cluster of fat" to simplify the discussion.

Fitting the normal distribution curve (the dashed line of figure 1) to the fat cluster, the whole angular distribution (dotted curve of figure 2) can be decomposed into normal fraction (the solid curve of figure 2) representing fat and the residual fraction shown as the dashed curve at the right in figure 2. The residual fraction is a mixed distribution corresponding to the enhancing tissues in the imaged subject. The significantly enhancing tissues are much more

heterogeneous than fat, and therefore fall in a number of small overlapping clusters. Using the decomposed distribution one can find the optimal threshold, α_0, discriminating between normal (fat) and residual populations using for example ROC technique [DJ Fink, D. Christiansen (editors), Electronics Engineers' Handbook, McGraw-Hill, 3rd edition, (1989): section 25 pp. 119-120].

Alternatively, one may wish to select a conservative threshold that discriminates only fat tissue without risk of loss of any valuable information. It is easy to see on figure 2 that the threshold corresponds to $\ln(\alpha) \approx -2.8$. The suppression of image effects caused by fat is done by replacing by a zero-vector the time-domain image vectors (uptake vectors) $\mathbf{Y}_i = (y_{i,1},\ldots,y_{i,M})$ in the time-sequence of separate image data sets (the matrix D below) which possess a value of the angle $\alpha < \alpha_0$ (i.e. replacement: $\mathbf{Y}_i \rightarrow (0,\ldots,0)$).

Alternatively, or additionally, the threshold may be determined and applied via a decomposition of the time-domain image vectors via a Principal Component Analysis (PCA) as follows.

Let D be a dynamic image matrix those columns are separates time-domain image vectors (uptake vectors) $\mathbf{Y}_i = (y_{i,1},\ldots,y_{i,M})$ for respective separates image pixel locations "i", and each row is formed from the complete contents of successive of the M separate datasets of the time-sequence, as follows

$$D = \begin{bmatrix} y_{1,1} & \cdots & y_{N,1} \\ \vdots & \ddots & \vdots \\ y_{1,M} & \cdots & y_{N,M} \end{bmatrix}$$

Let $p_j = (p_1,\ldots,p_M)$ **be** the j^{th} principal component (PC) vector and is the i^{th} column in P.

The value

$$Z_{j,i} = (p_j)'Y_i = \sum_{k=1}^{M} p_{j,k} \cdot y_{i,k}; \quad j = 1, \ldots, M; \quad i = 1, \ldots, N$$

is the value of the j^{th} principle component of i^{th} time-domain image vector (uptake vector).

The order of the principal component vectors in P depends upon the order of the corresponded eigenvalues (λ_k) thereof, such that $\lambda_1 > \lambda_2 > \ldots > \lambda_M$.

It has been found that second principal component is associated with the statistical measure (α), and that

these two quantities possess a strong negative correlation. Analysis of regression of the correlation of these two quantities has demonstrated that the value of the second principal component $Z_{2,i}=0$ approximates the value of the threshold α_0. It follows that if $Z_{2,i} > 0$ then the vector Y_i belongs to the "fat cluster"; otherwise the vector Y_i represents significantly enhancing tissue. (In other words, one may say that the above described "fat cluster" falls on the positive extent of the 2nd principal component.) In effect, the 2nd principle component is a statistical measure of enhancement equivalent to α. It should be understood that alternatives to the use of $Z_{2,i}=0$ as a threshold value (of 2nd principal component) could in principle be used. Figure 3 shows distributions of $\ln(\alpha)$ for populations classified as "fat" and "non-fat" using the described above PCA approach. One can see that the result coincides very well with the aforementioned conservative threshold technique illustrated in figure 2 (the whole distribution and the Gaussian distribution are also shown for comparison - not normalised).

It should be noted that if the aforementioned angular distribution method (α statistics) is employed, background noise (i.e. noise of empty background

surrounding the imaged subject) may obscure the optimal threshold, and therefore is preferably removed.

Figure 4 illustrates the effects upon the distribution of figure 1 of not removing background noise (the solid line of figure 4) from the distribution (such removal having occurred in the distribution of figure 1, reproduced as the dashed line in figure 4). However, one can see from figure 4 that the background noise overlaps mainly with the significantly enhancing tissues. The PCA approach is robust to the background noise.

The present invention may also permit as estimation of tissue-specific contrast enhancement effects as follows.

One may describe the time-domain image vector (uptake vector data) using the following linear model

$$\mathbf{Y}_i = B_i\mathbf{b} + H_i\mathbf{h}_k + \boldsymbol{\varepsilon}_i, \qquad i \in \Lambda_k, \qquad k = 1,2,... \tag{2}$$

The first term in eq. 2 is a baseline term. The second term describes the specific effect of cluster Λ_k, such that the vector $(B_i\mathbf{b} + H_i\mathbf{h}_k)$ is collinear with the centroid vector of the kth cluster, where $\boldsymbol{\mu}_k = (\mu_{k,1},...,\mu_{k,2})$ is the centroid vector whose components are the expectation

values $\mu_{k,1},\ldots,\mu_{k,2}$. The last term, $\boldsymbol{\varepsilon}_i$, is the residual vector. The vectors $\mathbf{b},\mathbf{h}_k$ are unit vectors. It is also required that $\mathbf{b}\perp\mathbf{h}_k\perp\boldsymbol{\varepsilon}_i$ for all i,k. It follows straightforwardly from the definition of the model that the residual term contains only random noise. Indeed, the random noise is defined as $\mathbf{Y}_i-\boldsymbol{\mu}_k$. According to the above discussion, $\boldsymbol{\varepsilon}_i\perp\boldsymbol{\mu}_k$ and, therefore, contains only the component of random noise that is orthogonal to $\boldsymbol{\mu}_k$. The complimentary component of noise (i.e. one collinear with $\boldsymbol{\mu}_k$) is spread across the first and second Principal Components (largest and next-largest) of the time-domain image vector (i.e. the first two terms of equation (3) below).

Existing subtraction imaging techniques define a baseline term as $Y_{i,1}\mathbf{1}$, where $Y_{i,1}$ is the first, pre-contrast point of the uptake vector Y_i and $\mathbf{1}$ is the identity vector. These existing techniques estimate the enhancement effect merely as $\mathbf{Y}_i-Y_{i,1}\mathbf{1}$, thereby leaving the noise "inside" the image data.

Compare the equation (2) with the following PCA decomposition of Y:

$$\mathbf{Y}_i = \sum_{n=1}^{M} Z_{n,i}\mathbf{p}_n \,, \qquad \mathbf{p}_1 \perp \ldots \perp \mathbf{p}_M \tag{3}$$

The PCA decomposition is a generic linear model of the data where the meaning of each particular term is unknown. However, by postulating equivalence of equation (2) and equation (3) one may assume that:

(1) the first Principal Component of the series in equation (3), namely the quantity $Z_{1,i}\ p_1$, is a "baseline" term;

(2) a few mid-Components describe the specific enhancement effect; and,

(3) the remaining Principal Components represents the noise which may be discarded from the PCA representation of Y_i .

Any suitable methods, such as would be readily apparent to the skilled person, may be employed to determine the most suitable value for the cut-off number $m < M$ being the value such that each j^{th} ($j > m$) principal component can be deemed to contain noise and can be "safely" discarded.

Thus the specific tissue effect (arising from significantly enhancing tissues) can be estimated using the following equation

$$Y^*_i = H_i\, h = \sum_{k=2}^{m} z_{k,i}\, p_k \qquad (4)$$

In effect this is subtraction of the baseline and residual terms of equation (2). Subtraction of this information from the time-domain image vectors will result in minimisation of the redundant information in the image vectors such that those vectors, and the information within them, therefore, represent substantially only the effects specific to tissue enhancement post-contrast.

Thus, the method of image processing may also include representing the time-domain image vector in terms of a principal component decomposition thereof employing all principal component vectors and corresponding principal component values thereof except: those principal component values thereof not exceeding a predetermined magnitude; and/or the largest principal component value thereof; and,

replacing by a value determined according to the principal component decomposition of the pixel value of each image data item of each of the plurality of the separate image data sets identified as being suitable for use in the generation of an image of the subject.

The invention, in a preferred embodiment, provides a method of processing a time-sequence of separate image data sets (each being either 2D or 3D) which records development of contrast enhancement in an imaged subject into which a contrast-enhancing agent has been introduced, the method containing some or all of the following steps:

1. PCA decomposition of the time-domain vector for each pixel location within the time-sequence of separate image data sets; followed by,
2. Suppression of image noise due to the random (and low-enhancing) effects (e.g. of fat) within an imaged subject as described above; followed by,
3. Estimation the specific enhancement effect by representing each time-domain image vector according to equation (4) (and optionally, the data can be de-noised removing a few last terms in the PCA series after estimation of the noise cut-off term number m).

It is to be understood that the present invention may provide means arranged to, or suitable for, the implementation of the image processing method of the invention. Accordingly, it is to be understood that the present invention encompasses such means.

The image processing may be performed on any suitable image processing means (e.g. a computer work station) which preferably includes image forming means for forming an image from image data having been processed by the image processing means according to the invention.

The invention may provide a computer program product (e.g. computer disk or other means for carrying/storing a computer program readable by a computer) containing a computer program for performing the processing method. The invention may provide a computer program for performing the method according to the invention.

Figure 5(a) shows the sequence of post-contrast images resulted from using the suggested approach. The background grey colour in each image outlines eliminated fatty tissue. The first image of the sequence on the left is a first post-injection image. Rest of the images are ordered according to their acquisition times from left to right. The image of the same subject generated according to known image subtraction techniques, and produced using the same sequence of datasets as that used for figure 5(a), is shown for comparison on figure 5(b). The time-sequence of datasets used for the example consists of seven image volumes: two pre- and five post-contrast,

performed after administration of Gd-DTPA. Temporal resolution was 90 sec. The data sets were acquired using 3D T1-weighted fast spoiled gradient echo sequence, on 1.5T Siemens scanner.

One can see granularities in the lesion and differences between tissues due to the contrast dynamics illustrated in figure 5(a) that are not seen on the corresponded subtracted image of figure 5(b). Comparison of these characteristics with ones of the anatomically identifiable tissues is used for understanding of the structure of the lesion. Figure 5(c) shows zoomed first image of the sequence of processed post-contrast images presented in figure 5(a). The dark area at the top of the lesion (pointed by the white arrow) was later identified as a blood vessel. The dark area at the centre (black arrow) is a compact region (shape has been assessed using an orthogonal display), and therefore most likely is part of the tumour that becomes enhanced later than the surrounding tissue.

Figures 6(a) and (b) show another example of an image processed according to the present invention (figure 6(a)) and one generated by simple subtraction of datasets (figure 6(b)). In figure 6(a) one can see a dark region in the middle of the lesion. This non-homogeneity is not

seen on the corresponding subtracted image of figure 6(b).

The method was initially valuated using 24 studies. In all the cases the approach has been shown more informative that the traditional subtracted image technique. Suppression of the ill-effects of fat upon a contrast-enhancement image significantly reduces the amount of data to be analysed. This results in faster and more reliable localisation of lesion, and the tumour contour is clearly defined. The method provides a capability of fast visual and reliable analysis of the data that is otherwise available only from analysis of individual uptake curves. Visualisation of differences in the dynamic contrast characteristics of the tissue provides a way for discrimination between tumour and blood vessels, and identification of granularities.

The complete elimination of the fatty tissue surrounding the lesion identifies the tumour's contour clearly, and provides a straightforward way for segmenting tumour extent and extracting features.

The method has been described in terms of Breast MR imaging. However, it can be applied to other types of

dynamic MR studies as will be readily apparent to the skilled person. Modifications and variants to the above embodiments, such as would be readily apparent to the skilled person, are encompassed within the scope of the present invention.

CLAIMS:

1. A method of processing a time-sequence of separate image data sets which record induced changes in pixel values of successive images of a subject, each set comprising a plurality of image data items which each represent the location of an image pixel of the image subject according to a common reference frame within which the subject is located, the method including the steps of:

(a) selecting from each of a plurality of said separate image data sets an image data item which represents an image pixel located at the same fixed image pixel location, thereby to generate a time-domain image data set;

(b) determining according to a predetermined measure of said induced changes as between the pixel values of the image data items of the time-domain image data set whether the image data items thereof are associated with the presence of a specified material within the image subject.

2. A method according to Claim 1 including an additional step (c), following step (b), of identifying the image data items of the time-domain image data set as being unsuitable for use in the generation of an image of

the subject after having been identified in step (b) as associated with the presence of the specified material within the image subject if the specified material is of a type which it is not desired to be included within the image of the subject.

3. A method according to Claim 1 or 2 wherein the predetermined measure is defined according to a measure of the dispersion of the values of pixel intensity associated with the image data items within the time-domain image data set.

4. A method according to Claim 1, 2 or 3 wherein the image data items of the time-domain image data set are determined as being associated with the presence of the specified material within the image subject if the predetermined measure exceeds a predetermined threshold value.

5. A method according to any preceding claim in which step (b) includes:

forming a time-domain image vector wherein each image data item of the time-domain image data set represents a separate vector component of an array of vector components arranged in said time-sequence to form the time-domain image vector;

determining the measure of dispersion according to a property of the time-domain image vector in vector space.

6. A method according to Claim 5 wherein the measure of dispersion is determined according to the degree to which a time-domain image vector differs from an identity vector in the same vector space.

7. A method according to Claim 6 including:

determining the angle (α) subtended by the time-domain image vector with respect to the identity vector in the vector space of the time-domain image vector; and,

employing said angle (α) as the predetermined measure, wherein the predetermined threshold value is a predetermined value of the predetermined measure.

8. A method according to Claim 7 wherein said predetermined threshold value is exceeded if said angle (α) is less than a threshold angle value (α_0).

9. A method according to Claim 7 or 8 including:

repeating step (a) in respect of a plurality of image data items thereby to generate a corresponding plurality of time-domain image data sets;

forming a corresponding plurality of time-domain image vectors with each image data item of a given time-

domain image data set representing a separate vector component of an array of vector components arranged in said time-sequence to form the given time-domain image vector;

determining the angle subtended by each of said time-domain image vectors with respect to the identity vector in the vector space of the time-domain image vector; and,

determining from the distribution of the values of said angles of all of said time-domain vectors the portion of said angular distribution arising substantially only from the presence within the image subject of said specified material, wherein said predetermined threshold value is exceeded if the said angle subtended by said time-domain image vector falls within said portion of said angular distribution.

10. A method according to Claim 9 wherein said threshold angle value (α_0) is the angular value which demarcates the portion of the angular distribution arising substantially only from the presence within the image subject of said specified material from the other portion(s) of the angular distribution.

11. A method according to Claim 9 or 10 wherein the

angular distribution is the distribution of the natural logarithm of the value of the angles, and said portion of said angular distribution arising substantially only from the presence within the image subject of said specified material is determined according to a Normal Distribution having distribution parameters which cause it to most closely correspond with a portion of said angular distribution.

12. A method according to Claim 5 including:

determining the second principal component of the time-domain image vector; and,

employing the value of said second principal component as said predetermined measure, wherein the predetermined threshold value is a predetermined value of the predetermined measure.

13. A method according to Claim 12 wherein the predetermined threshold value is exceeded if the value of the second principal component is greater than zero.

14. A method according to any of preceding claims 2 to 13 including the additional step of:

(d) replacing by a value of zero the pixel value of each image data item of each of said plurality of said

separate image data sets identified as being unsuitable for use in the generation of an image of the subject.

15. A method according to any preceding claim including:

representing the time-domain image vector in terms of a principal component decomposition thereof employing all principal component vectors and corresponding principal component values thereof except: the largest principal component value thereof; and those principal component values thereof not exceeding a predetermined magnitude;

replacing by a value determined according to said principal component decomposition the pixel value of each image data item of each of said plurality of said separate image data sets identified as being suitable for use in the generation of an image of the subject.

16. A method according to any of preceding claims 2 to 15 in which steps (a) to (c) are repeated in respect of each pixel of each of said time-sequence of separate image data sets.

17. A method according to any preceding claim

including forming an image from image data comprised in said time-sequence of separate image data sets having been processed according to any preceding claim.

18. Image processing means for processing a time-sequence of separate image data sets which record induced changes in pixel values of successive images of a subject, each set comprising a plurality of image data items which each represent the location of an image pixel of the image subject according to a common reference frame within which the subject is located, the image processing means including:

(a) selection means for selecting from each of a plurality of said separate image data sets an image data item which represents an image pixel located at the same fixed image pixel location, thereby to generate a time-domain image data set;

(b) decision means for determining according to a predetermined measure of said induced changes as between the pixel values of the image data items of the time-domain image data set whether the image data items thereof are associated with the presence of a specified material within the image subject.

19. The image processing means according to Claim

18 including identifying means arranged to identify the image data items of the time-domain image data set as being unsuitable for use in the generation of an image of the subject if they are identified by said decision means (b) as being associated with the presence of the specified material within the image subject and if the specified material is of a type which it is not desired to be included within the image of the subject.

20. Image processing means according to Claim 18 or 19 wherein the predetermined measure is defined according to a measure of the dispersion of the values of pixel intensity associated with the image data items within the time-domain image data set.

21. Image processing means according to Claim 18, 19 or 20 wherein the image data items of the time-domain image data set are determined as being associated with the presence of the specified material within the image subject if the predetermined measure exceeds a predetermined threshold value.

22. Image processing means according to any of preceding claims 18 to 21 in which said decision means includes:

vector means arranged to form a time-domain image vector wherein each image data item of the time-domain image data set represents a separate vector component of an array of vector components arranged in said time-sequence to form the time-domain image vector;

dispersion determining means arranged to determine the measure of dispersion according to a property of the time-domain image vector in vector space.

23. Image processing means according to Claim 22 wherein measure of dispersion is determined according to the degree to which a time-domain image vector differs from an identity vector in the same vector space.

24. Image processing means according to Claim 23 including:

angle determining means arranged to determine the angle (α) subtended by the time-domain image vector with respect to the identity vector in the vector space of the time-domain image vector; and,

said decision means is arranged to employ said angle (α) as the predetermined measure, wherein the predetermined threshold value is a predetermined value of the predetermined measure.

25. Image processing means according to Claim 24 wherein said predetermined threshold value is exceeded if said angle (α) is less than a threshold angle value (α_0).

26. Image processing means according to Claim 18 wherein said selection means is arranged to generate in respect of a plurality of image data items a corresponding plurality of said time-domain image data sets;

said vector means is arranged to form a corresponding plurality of time-domain image vectors with each image data item of a given time-domain image data set representing a separate vector component of an array of vector components arranged in said time-sequence to form the given time-domain image vector;

said angle determining means is arranged to determine the angle subtended by each of said time-domain image vectors with respect to the identity vector in the vector space of the time-domain image vector; and,

said decision means is arranged to determine from the distribution of the values of said angles of all of said time-domain vectors the portion of said angular distribution arising substantially only from the presence of a specified material within the image subject, wherein said predetermined threshold value is exceeded if the

said angle subtended by said time-domain image vector falls within said portion of said angular distribution.

27. Image processing means according to Claim 26 wherein said threshold angle value (α_0) is the angular value which demarcates the portion of the angular distribution arising substantially only from said specified material from the other portion(s) of the angular distribution.

28. Image processing means according to Claim 26 or 27 wherein the angular distribution is the distribution of the natural logarithm of the value of the angles, and said decision means is arranged to determine said portion of said angular distribution arising substantially only from said specified material according to a Normal Distribution having distribution parameters which cause it to most closely correspond with a portion of said angular distribution.

29. Image processing means according to Claim 22 including:

principal component means arranged to determine the second principal component of the time-domain image vector; and,

said decision means is arranged to employ the value of said second principal component as said predetermined measure, wherein the predetermined threshold value is a predetermined value of the predetermined measure.

30. Image processing apparatus according to Claim 29 wherein the predetermined threshold value is exceeded if the value of the second principal component is greater than zero.

31. Image processing means according to any of preceding claims 18 to 30 including:

(d) data modifying means arranged to replace by a value of zero the pixel value of each image data item of each of said plurality of said separate image data sets identified as being unsuitable for use in the generation of an image of the subject.

32. Image processing means according to any of preceding claims 18 to 31 wherein said principal component means is arranged to represent the time-domain image vector in terms of a principal component decomposition thereof employing all principal component vectors and corresponding principal component values thereof except: the largest principal component value

thereof; and those principal component values thereof not exceeding a predetermined magnitude;

the image processing means including data modifying means arranged to replace by a value determined according to said principal component decomposition the pixel value of each image data item of each of said plurality of said separate image data sets identified as being suitable for use in the generation of an image of the subject.

33. Image processing means according to any of preceding claims 18 to 32 arranged to so process each pixel of each of said time-sequence of separate image data sets.

34. Image processing means according to any of preceding claims 18 to 33 including image forming means for forming an image from image data comprised in said time-sequence of separate image data sets having been processed by said image processing means according to any preceding claim.

35. Image processing means according to any one of preceding claims 18 to 34 comprising computer means programmed to perform the method according to any one of claims 1 to 17.

36. Computer means programmed to perform the method according to any one of claims 1 to 17.

37. A computer program product containing a computer program for performing the method according to any one of claims 1 to 17.

38. A computer program for performing the method according to any one of claims 1 to 17.

39. An image generated according to the method of any one of claims 1 to 17.

40. A method substantially as described in any one embodiment hereinbefore with reference to the accompanying drawings.

41. Image processing means substantially as described in any one embodiment hereinbefore with reference to the accompanying drawings.

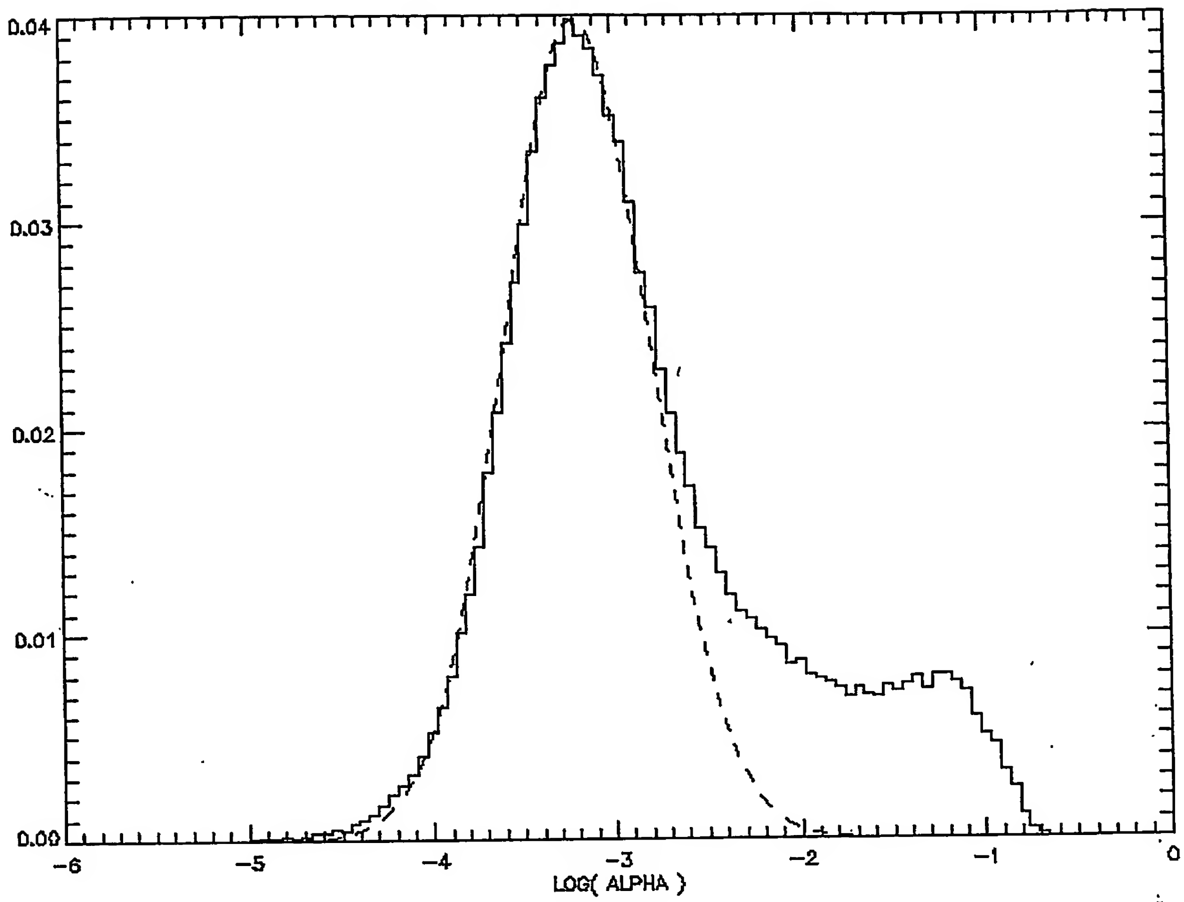


Figure 1

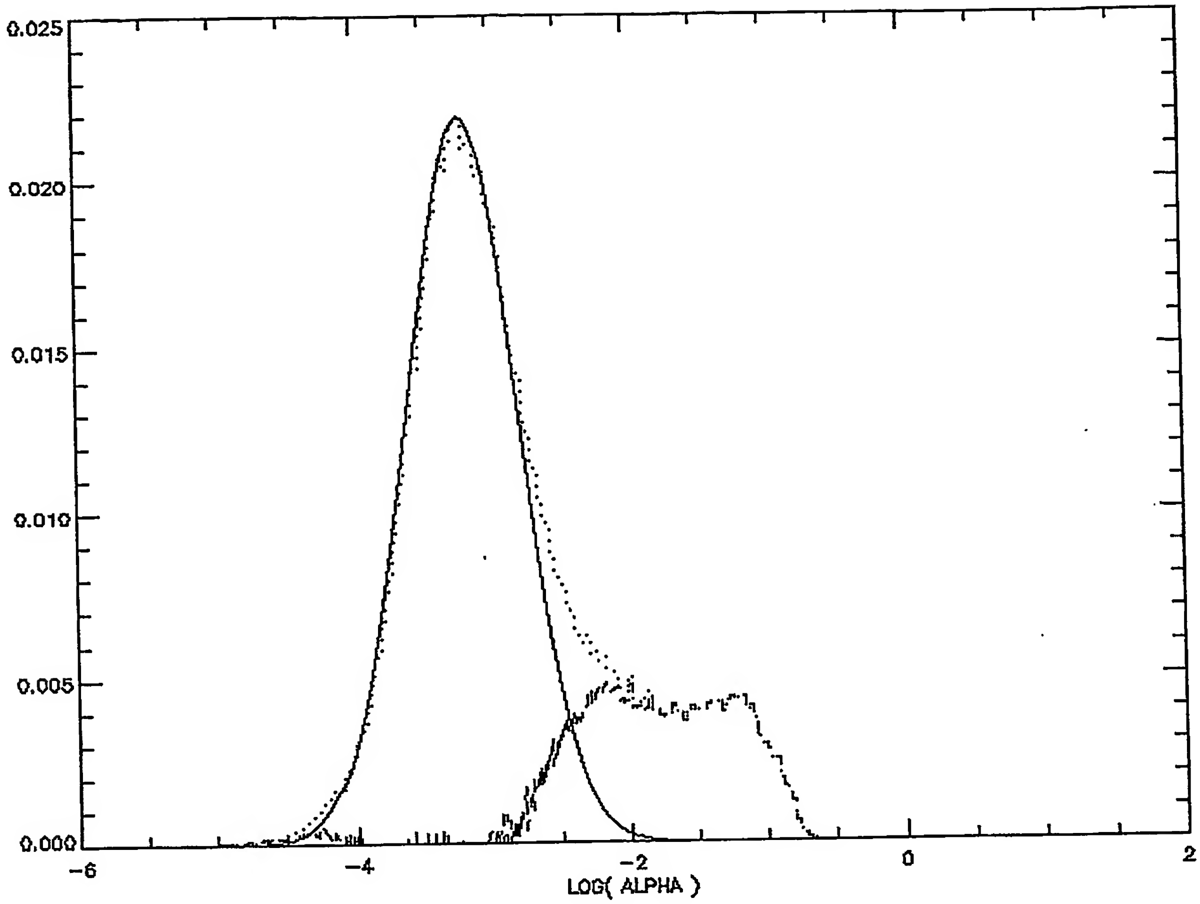
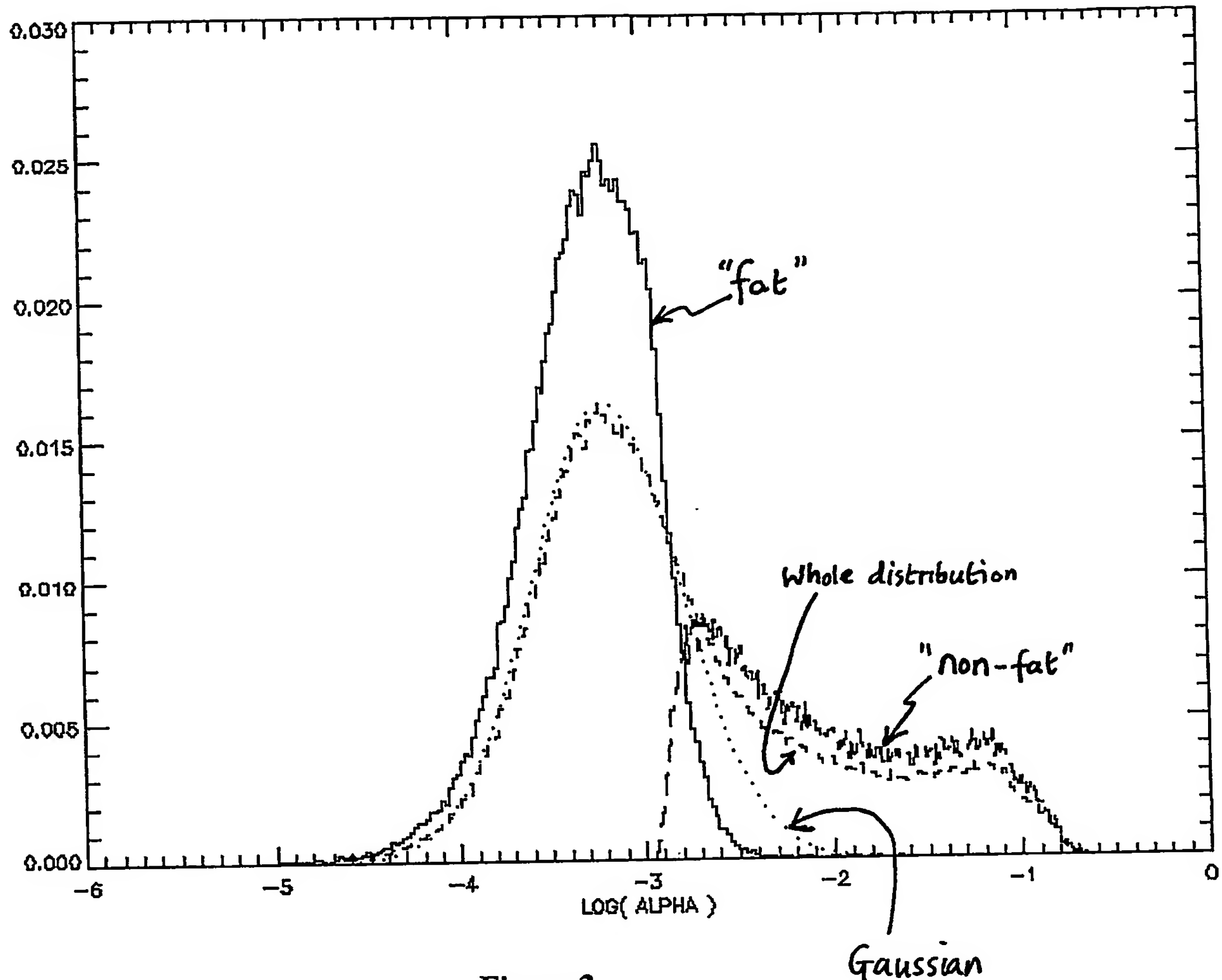
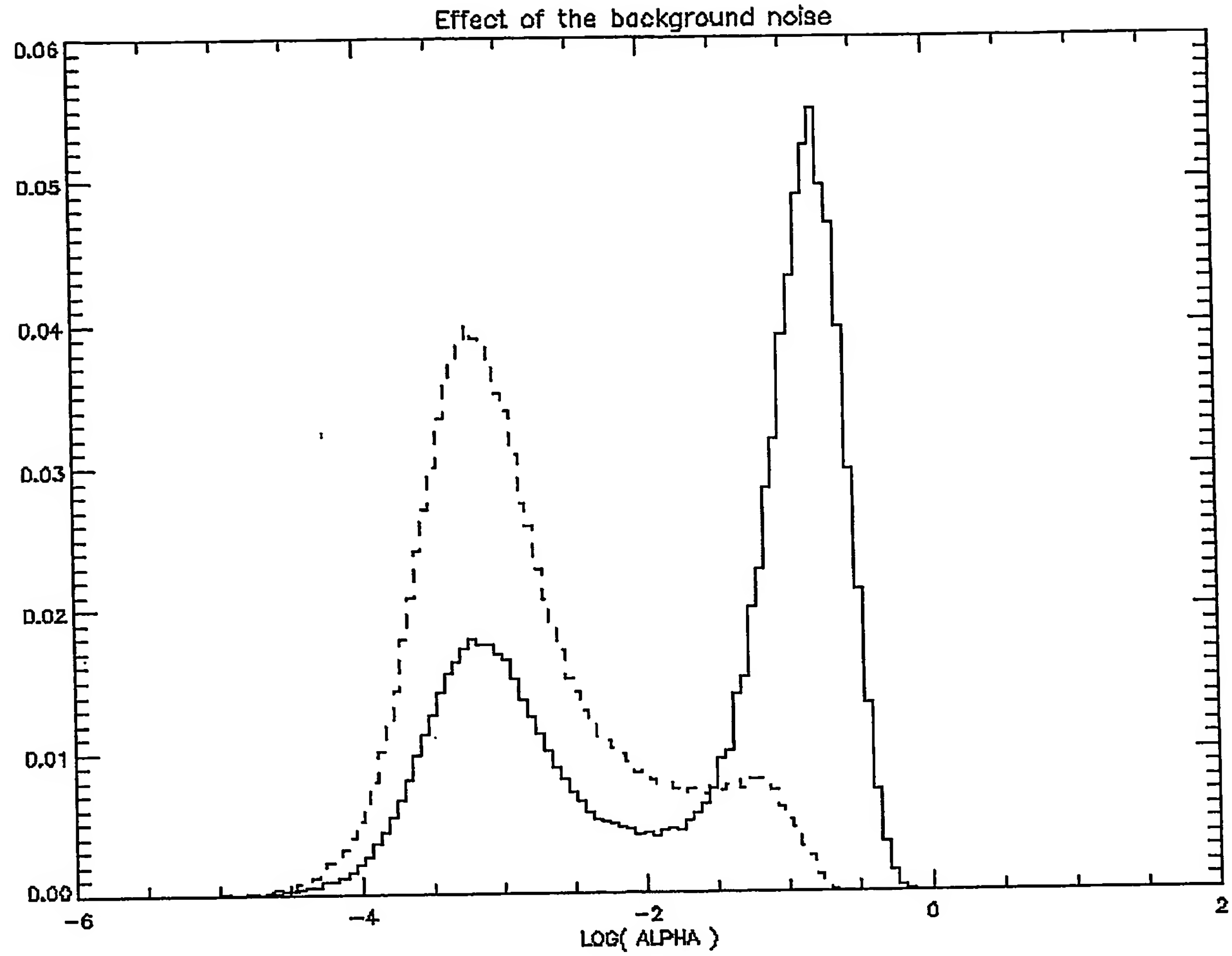


Figure 2



0.030
0.025
0.020
0.015
0.010
0.005
0.000
-6
-5
-4
-3
-2
-1
0
LOG(ALPHA)
"fat"
Whole distribution
"non-fat"
Gaussian

Figure 3



Effect of the background noise
0.06
0.05
0.04
0.03
0.02
0.01
0.00
−6
−4
−2
0
2
LOG(ALPHA)

Figure 4

Figure 5(a)

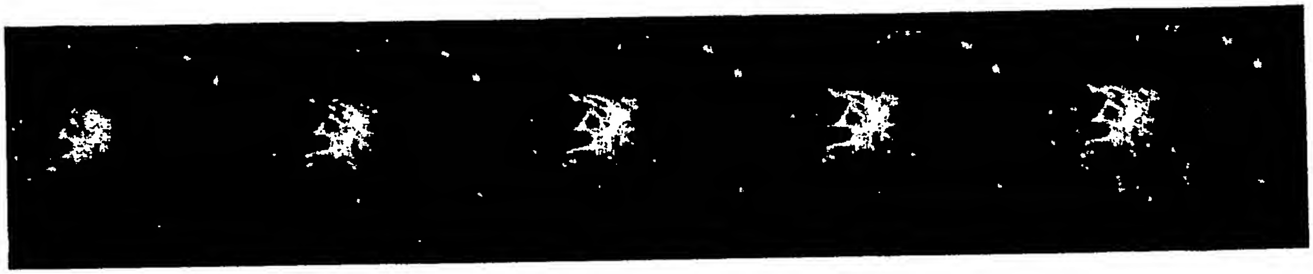


Figure 5(b)

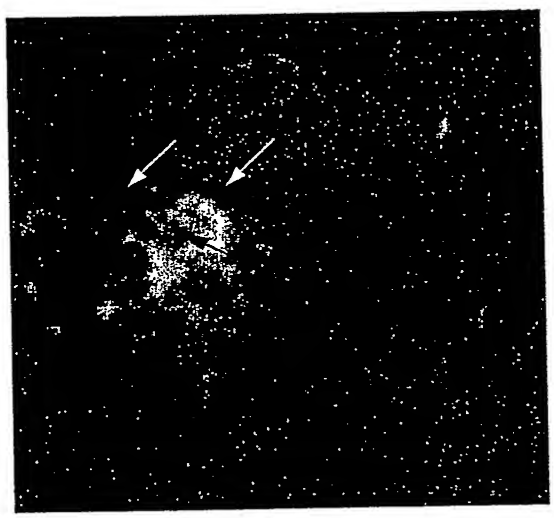


Figure 5(c)

Figure 6(a)

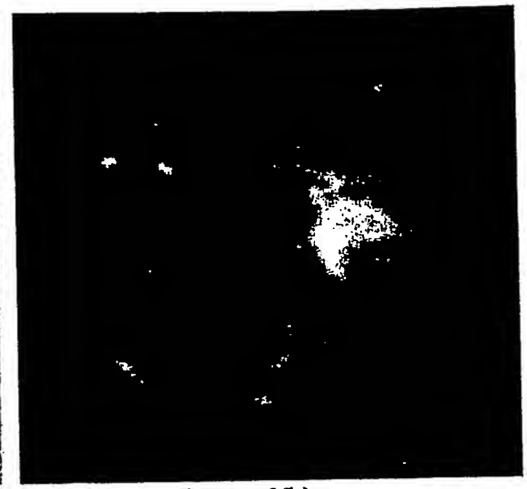


Figure 6(b)

NOT TO BE AMENDED

This Page is Inserted by IFW Indexing and Scanning Operations and is not part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- ☐ BLACK BORDERS
- ☑ IMAGE CUT OFF AT TOP, BOTTOM OR SIDES
- ☑ FADED TEXT OR DRAWING
- ☑ BLURRED OR ILLEGIBLE TEXT OR DRAWING
- ☐ SKEWED/SLANTED IMAGES
- ☐ COLOR OR BLACK AND WHITE PHOTOGRAPHS
- ☐ GRAY SCALE DOCUMENTS
- ☑ LINES OR MARKS ON ORIGINAL DOCUMENT
- ☐ REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY
- ☐ OTHER: ______________________

IMAGES ARE BEST AVAILABLE COPY.
As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.